



Galactooligosaccharides and Human Health Implications



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Abstract

Galactooligosaccharides (GOS) are non-digestible oligosaccharides which show several physiological properties. The major physiological characteristic is associate with its importance to promote the health of human gut microflora. GOS are formed from concentrated lactose solutions by transgalactosylation reaction of β -galactosidase enzyme. The galactooligosaccharides are prebiotics because promote beneficial effects on microflora and are recognized with the GRAS status. These prebiotics can be incorporated in several products as infant formula, beverages, dairy products, and bakery and confectionary foods. The present mini review aims report about galactooligosaccharides and its relationship with human health.

Keywords: Prebiotics; Bifidobacteria and lactobacilli; GRAS status; Physiological effects; Gut microflora

Abbreviation: GOS: Galactooligosaccharides; TOS: Transgalac-tooligosaccharides; NDO: Non-Digestible Oligosaccharides; FDA: Food and Drug Administration

Introduction

Functional foods have been studied for many researchers around the world principally, due its relationship with benefits positive to health human. The functional foods originated in Japan in the 1980s consist of natural or processed food that contains bioactive compounds and consequently provide a clinically proven and documented health benefit for the prevention, management, or treatment of chronic disease. Among the various functional foods, one of the most important are galactooligosaccharides (GOS), non-digestible oligosaccharides that show as main physiological effect an increase the beneficial microflora of the intestine. GOS are prebiotic and synthesized by the β -galactosidase enzyme, in a reaction known as transgalactosylation. These prebiotics can be used in a variety of food such as infant milk formula, fruit juices, meal replacers, fermented milks, bread and confectionary products. The GOS prebiotics thus, can contribute directly and efficiently with the intestinal flora. This review aimed at pointing to relationship between GOS and implications on human health.

Oligosaccharides

Oligosaccharides, which have from two to ten saccharide units, linked covalently by glycoside bonds in their molecular structure, include maltooligosaccharides and other oligosaccharides [1]. Many oligosaccharides are not digestible by the human organism, others are partially hydrolyzed in the gastrointestinal tract and can result in the formation of essential carbohydrates for health and act as substrates and regulators of the major metabolic pathways [2]. The monosaccharides resulting from this partial hydrolysis are transported through the blood to the liver and later to the systemic circulation. Non-digestible oligosaccharides (NDO) occur naturally in several foods and plant tissues and can be synthesized in the metabolism of animals and microorganisms [3,4]. The oligosaccharides are obtained by extraction of plant tissues, by microbial fermentation, by enzymatic catalysis or by chemical reaction [5]. The physiological and physicochemical properties of its components have been reported as equivalent to dietary fibers, associating their physiological action with important aspects of human health [6]. Due to these properties,

oligosaccharides are considered a class of active biomolecules of great importance for human health and are being explored industrially in the development of functional food [4].

Functional Food

The Functional Food Center (FFC) describe that functional food may be natural or processed food with known or unknown biologically active compounds and that provide a clinically proven and documented health benefit for the prevention, management or treatment of chronic disease [7]. Food and Drug Administration (FDA) does not provide a statutory definition of functional foods. At 1990, Nutrition Labeling and Education authorized the FDA to develop regulations for the use of claims on health benefits on foods and dietary supplements, which are often communicated to the consumers through the label on the product, website, or advertising [8]. Functional foods can be regulated as a conventional food, a dietary supplement, a food for special dietary use, a medical food, or a drug and often these distinctions are based depending on the intended use and nature of the claim(s) (e.g., nutrient information and nutrient content and health claims) made on the product. Nutrition and health claims are used to communicate the benefits of functional foods. Within these specifications are the GOS prebiotics.

Galactooligosaccharides (GOS)

GOS, also known as oligogalactosyllactose, oligogalactose, oligolactose, or transgalactooligosaccharides (TOS) are non-digestible carbohydrate, resistant to intestinal digestive enzymes with fiber-like effects found naturally in breast milk [9]. Galactooligosaccharides are formed from concentrated lactose solutions by transgalactosylation reaction of β -galactosidase enzyme. β -galactosidase enzyme has similar affinity for both hydrolysis and lactose transgalactosylation [10,11]. The major physiological effect is the selective proliferation of beneficial bacteria especially bifidobacteria and lactobacilli in the gut, which provide resistance against colonization of pathogens thereby reducing exogenous and endogenous intestinal infections [12]. The physico chemical characteristics are associate with water solubility, colorless, viscosity like high-fructose corn syrup, stable to 160 °C for 10min at pH 7; stable to 100 °C for 10 min at pH 2; stable to 37 °C at pH 2 for several months, reduces the freezing point of foods, humectant properties and sweetness from 0.3 to 0.6 times more of sucrose [13]. By presenting these properties, the GOS can be used in production various foods such as infant formula, beverages, bakery products, pet foods and confectionary products.

Synthesis of GOS

The synthesis of GOS involves three main steps: first, there is the formation of the enzyme-galactosyl complex, followed by hydrolysis of the glycosidic bond $\beta 1 \rightarrow 4$ of lactose and the simultaneous release of glucose. Then, enzyme-galactosyl

complex is transferred to nucleophilic acceptors containing a hydroxyl group (water or saccharides). In solutions, with low lactose concentration, this acceptor is water, resulting in the formation of galactose. In concentrated lactose solutions, the disaccharide acts as an acceptor and binds to the enzyme-galactosyl complex resulting in the formation of galactooligosaccharides [14]. The rate of GOS production formed is influenced by several factors such as enzyme source, reaction time, pH, process temperature, initial concentration of lactose and the presence of specific inhibitors or activators for the enzyme [15]. In general, and in this case, higher lactose concentration in the medium, higher GOS yield, since, after hydrolysis, the final acceptor of the β -galactosyl group becomes the lactose molecule itself instead of water [16]. The GOS commercially available are founded in liquid or powder forms, and are mixtures of several species of oligosaccharides, lactose, glucose and small amount of galactose. In the Japanese market, we can find the Oligomate 55 product which contains at least 55% 4'-GOS. The Oligomate commercial products offer mainly GOS with $\beta 1 \rightarrow 6$ linkages; the Bimuno contains mainly $\beta 1 \rightarrow 3$ linkages, Cup-Oligo mainly $\beta 1 \rightarrow 4$ linkages. GOS have a generally recognized as safe (GRAS) status because its components are originated from human milk and yoghurt and are produced from ingested lactose by resident intestinal bacteria which produce β -galactosidase [17].

GOS and Human Health Implications

GOS show two major benefit to health human: selective proliferation of beneficial bacteria especially bifidobacteria and lactobacilli in the gut, which provide resistance against colonization of pathogens thereby reducing exogenous and endogenous intestinal infections and by production of short chain fatty acids show various beneficial effects including reduction of cancer risk, increase in mineral absorption, improvement in bowel habit, control of serum lipid and cholesterol level, and reduce cancer risk and IBD inflammation [18,19]. GOS are included among non-digestible oligosaccharides (NDOs) that have prebiotic properties and are licensed as FOSHU (Foods for Specified Health Use) food additives by the Japanese Ministry of Health [19]. In the late 1970s, the use of GOS as substitute milk oligosaccharides in infant formulas was proposed with the aim of promoting healthy intestinal microflora [19]. Many studies have reported about the GOS potential in human health promotion. Scholtens et al. [20] administered galactooligosaccharide and fructooligosaccharide (FOS) doses to 38 infants for 6 weeks and demonstrated the increase of bifidobacteria in the intestinal microbiota. Bruzzese et al. [21] also performed a study with 342 infants using GOS and FOS (0.4g/100mL/day) and reported the reduction of respiratory and intestinal infections during the first year of life. Vulevic [22] evaluated the ability of GOS to reduce markers of metabolic syndrome. Forty-five volunteers with overweight and three risk factors

for the syndrome were selected. In a double-blind study, volunteers ingested 5.5g/day of GOS for 6 and 12 weeks, control was performed with placebo. The author concluded that ingestion of GOS increased the population of bifidobacteria and decreased bacteroides and *Clostridium histolyticum* when compared with placebo. Musilova et al. [23] evaluated the effect of the combination of GOS and maltodextrin in vitro by incubating in fecal samples, and in vivo by administration of maltodextrin in healthy adults, followed by analysis of the microbiota fecal. In the in vitro test, a greater amount of bifidobacteria was observed. In the in vivo analyzes, the increase of fecal bifidobacteria was approximately 30 % and the reduction of *Escherichia coli* was around 20%. Thus, the authors concluded that the mixture of GOS and maltodextrin promoted bifidogenic properties, promoted the growth of bifidobacteria and inhibited the development of undesirable bacteria. A recent study, Perdijk et al. [24] investigated the effects of the human milk oligosaccharides (HMO) sialyllactose (SL), and galactooligosaccharides (GOS) on epithelial barrier functioning, microbiota composition, and short chain fatty acids (SCFA) production and concluded SL and GOS did show distinct modulation of microbiota composition, promoting the outgrowth of *Bacteroides* and bifidobacteria, respectively, which resulted in distinct changes in SCFA production profiles.

Conclusion

This article provides a mini review about galactooligosaccharides and its relationship with human health. The galactooligosaccharides (GOS) are non-digestible oligosaccharides and synthesized by β -galactosidase enzyme in a reaction known as transgalactosylation. GOS are prebiotics that show as major physiological effect because alter the balance of the large bowel microbiota by increasing bifidobacteria and *Lactobacillus* number. These prebiotics are recognized as GRAS status and then, can be used in a several foods including kid's formula milk, fermented milk, confectionary products, breads and others.

References

1. Mehra R Kelly P (2006) Milk oligosaccharides: structural and technological aspects. *International Dairy Journal* 16 (11): 1334-1340.
2. Macfarlane GT, Steed H, Macfarlane S (2008) Bacterial metabolism and health-related effects of galactooligosaccharides and other prebiotics. *J Appl Microbiol* 104(2): 305-344.
3. Roberfroid M, Slavin J (2000) Nondigestible oligosaccharides. *Crit Rev Food Sci Nutr* 40(6): 461-480.
4. Van Loo J, Cummings J, Delzenne N, Englyst H, Franck A, et al. (1999) Functional food properties of non-digestible oligosaccharides: a consensus report from the ENDO project (DGXII AIRII-CT94-1095). *British Journal of Nutrition* 81 (2): 121-132.
5. Mussato S L Mancilha I M (2007) Non-digestible oligosaccharide: a review. *Carbohydrate Polymers* 68(3): 587-597.
6. Nakakuki T (2002) Present status and future of functional oligosaccharide development in Japan. *Pure and Applied Chemistry* 74(7): 1245-1251.
7. Martirosyan DM, Singh J A (2015) New definition of functional food by FFC: what makes a new definition unique?. *Functional Foods in Health and Disease* 5 (6): 209-223.
8. FDA Regulation. U.S. Food and Drug Administration. Guidance for Industry: Evidencebased review system for the scientific evaluation of health claims - Final.
9. Moro GE, Stahl B, Fanaro S, Jelinek J, Boehm G, et al. (2005) Dietary prebiotic oligosaccharides are detectable in the faeces of formula-fed infants. *Acta Paediatrica* 94(449): 27-30.
10. Torres D, Gonçalves M, Teixeira J, Rodrigues L (2010) Galacto-oligosaccharides: production, properties, applications, and significance as prebiotics. *Comprehensive Reviews in Food Science and Food Safety* 9(5): 438-454.
11. Jurado E, Camacho F, Luzón G, Vicaria JM (2002) A new kinetic model proposed for enzymatic hydrolysis of lactose by β -galactosidase from *Kluyveromyces fragilis*. *Enzyme and Microbial Technology* 31: 300-309.
12. Schwab C, Ganzle M (2011) Lactic acid bacteria fermentation of human milk oligosaccharide components, human milk oligosaccharides and galactooligosaccharides. *FEMS Microbiology Letters* 315(2): 141-148.
13. Sangwan V, Tomar SK, Singh RR, Singh AK, Ali B (2011) Galactooligosaccharides: Novel Componentsof Designer Foods. *J Food Sci* 76(4): R103-R111.
14. Prenosil JE, Stuker E, Bourne JR (1987) Formation of oligosaccharides during enzymatic lactose hydrolysis and their importance in a whey hydrolysis process: Part II. Experimental. *Biotechnol Bioeng* 30(9): 1026 -1031.
15. López-Eiva MH, Guzman M (1995) Formation of oligosaccharides during enzymatic hydrolysis of milk whey permeates. *Process Biochemistry* 30(8): 757-762.
16. Gosling A, Stevens GW, Barber AR, Kentish SE, Gras SL (2011) Effect of the substrate concentration and water activity on the yield and rate of the transfer reaction of β - galactosidase from *Bacillus circulans*. *Journal of Agricultural and Food Chemistry* 59(7): 3366-3372.
17. Spherix Consulting Inc (2010) Generally Recognized as Safe (GRAS) determination for the use of galacto-oligosaccharides in foods and infants' formulas. Yakult Pharmaceutical Industry Co., Ltd, Kunitachi-shi.
18. Broek L A M V D Hinz S W A Beldman G Vincken J P Voragen A G J (2008) Bifidobacterium carbohydrases their role in breakdown and synthesis of (potential) prebiotics. *Mol Nutr Food Res* 52(1):146-63.
19. Tzortzis G, Vulevic J (2009) Galactooligosaccharide prebiotics, In: Prebiotics and Probiotics: Science and Technology. In: Charalampopoulos D & Rastall RA, (Eds.), Springer Science, New York, pp. 207-244.
20. Scholtens PA, Alles MS, Bindels JG, Van Der Linde EG, Tolboom JJ, et al. (2006) Efeitos bifidogênicos de alimentos sólidos de desmame com adição de oligossacarídeos prebióticos: um ensaio clínico controlado randomizado. *Journal of Pediatric Gastroenterology and Nutrition* 42(5): 553-559.
21. Bruzzese E, Volpicelli M, Squeglia V, Bruzzese D, Salvini F, et al. (2009) Uma fórmula contendo galacto e fruto-oligosacarídeos previne infecções intestinais e extra-intestinais: um estudo observacional. *Clinical Nutrition (Edimburgo, Escócia)* 28(2): 156-161.
22. Vulevic J, Drakoularakou A, Yaqoob P, Tzortzis G, Gibson GR (2008) Modulação do perfil da microflora fecal e função imune por uma nova mistura trans-galactooligosacarídeo (B-GOS) em voluntários idosos saudáveis. *American Journal of Clinical Nutrition* 88(5): 1438-1446.
23. Musilova S, Rada V, Marounek M, Nevorál J, Dusková D, et al. (2015) Prebiotic effects of a novel combination of galactooligosaccharides and maltodextrins. *Journal of Medicinal Food* 18(6): 685-689.

24. Perdijk O, van Baarlen P, Fernandez-Gutierrez MM, van den Brink E, Schuren FHJ, et al. (2019) Sialyllactose and Galactooligosaccharides Promote Epithelial Barrier Functioning and Distinctly Modulate Microbiota Composition and Short Chain Fatty Acid Production *In Vitro*. *Front Immunol* 12: 10:94.



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